REMARKS

As a result of the foregoing amendments, Claim 5 has been canceled, and Claim 1 has been amended to include the limitations of canceled Claim 5. Now canceled Claim 5 required that the cells to be cultured be obtained by surgical resection from a patient. Claim 1 has also been amended to recite that the cells obtained by surgical resection are a mixture of astrocytes and microglial cells (as supported by the Specification in the second paragraph of page 2) and that the resected cells are dissociated (see Example 1.1, starting on page 21 of the Specification). No new matter has been entered by way of these amendments.

Claims 14-32 have been withdrawn from further consideration as being drawn to a non-elected invention. Accordingly, claims 1-4 and 6-13 are now being examined.

Claims 1-6 and 13 are Not Anticipated

Applicants respectfully traverse the rejection of claims 1 – 6 and 13 under 35 U.S.C. 102(b) as being anticipated by De Groot *et al.* (1977) "Establishment of Human Adult Astrocyte Cultures Derived from Postmortem Multiple Sclerosis and Control Brain and Spinal Cord Regions: Immunophenotypical and Functional Characterization" J Neuroscience Res. 49:342-54 (hereinafter "De Groot"). De Groot teaches a preliminary step specifically for removing microglial cells from the astrocyte culture, and that step is excluded by amended Claim 1 and all claims which depend from Claim 1. Accordingly, the claimed process for producing an essentially pure culture of astrocytes is not anticipated by the disclosure of De Groot.

De Groot teaches a method of isolating a culture of astrocytes, wherein resected spinal cord or brain tissues were mechanically dissociated and then "... to avoid contamination of the astrocyte cultures ..." the cell suspension was plated onto uncoated tissue culture flasks and incubated for 2 hours. "This step allows monocytes/macrophages to adhere to the bottom of the flasks. Subsequently, 10 ml of the supernatant containing dissociated [astrocyte] cells and myelin debris was plated into [new flasks] ...," De Groot, p. 344, first column. Microglial cells are one type of macrophage (see Dorland's Illustrated Dictionary, 27th Edition – copy of title page and definition of macrophage attached). Only after this procedure was the astrocyte-containing supernatant plated on flasks to which the astrocytes could adhere for 48 hours.

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In contrast, the instant claims require that the dissociated cells of the resection be incubated *directly* on a flask under conditions enabling attachment of the astrocytes to the flask. Accordingly, the instant claims exclude the 2-hour incubation on an untreated flask step taught by De Groot specifically for the purpose of removing macrophage, and therefore microglial, cell contaminants. For this reason, the instant claims are not anticipated by De Groot under 35 U.S.C. 102 (b). Reconsideration and withdrawal of this rejection are respectfully requested.

Claims 7-12 are Non-obvious

Applicants respectfully traverse the rejection of claims 7-12 under 35 U.S.C. 103(a) as being unpatentable over De Groot in view of US 5,627,047 and US 5,202,120. Rejected claims 7-12 all depend from Claim 1. As discussed above, De Groot teaches a different step for the removal of microglial cell contaminants from the astrocyte culture, and that step is excluded by amended Claim 1. Since De Groot specifically teaches the instantly excluded step to be necessary for the removal of microglial cells, there is no teaching, suggestion or motivation in that reference that would lead one of skill in the art of microbiology to exclude the De Groot step and thereby arrive at the instantly claimed process. Furthermore, nothing in US 5,627,047 or US 5,202,120 teaches, suggests or motivates one of skill in the art to exclude the De Groot step and thereby arrive at the instantly claimed process. Accordingly, the combination of De Groot, US 5,627,047 and US 5,202,120 fail to teach or suggest the instantly claimed process. Reconsideration and withdrawal of this rejection are respectfully requested.

Respectfully submitted,

F. Aaron Dubberley, Reg. No. 41,001
Attorney/Agent for Applicant

Aventis Pharmaceuticals Inc.
Patent Department
Route #202-206 / P.O. Box 6800
Bridgewater, New Jersey 08807-0800
Telephone: 908-231-3737
Telefax: 908-231-2626

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27th Edition

DORLAND'S ILLUSTRATED

Medical Dictionary

1988

W.B. SAUNDERS COMPANY
Harcourt Brace Jovanovich, Inc.

Philadelphia London Toronto
Montreal Sydney Tokyo

macrolide (mak'ro-līd) 1. a chemical compound characterized by a large lactone ring containing multiple keto and hydroxyl groups. 2. any of a group of antibacterial antibiotics (e.g., erythromicin or oleandomycin) containing a macrolide ring linked glycosidically to one or more sugars. Macrolides are produced by certain species of *Streptomyces* and inhibit protein synthesis by binding to the 50S subunits of 70S ribosomes.

macrolymphocyte (mak"ro-lim'fo-sīt) a large lymphocyte.

macrolymphocytosis (mak-ro-lim"fo-si-to'sis) the presence of an increased number of large lymphocytes.

macromastia (mak"ro-mas'te-ah) [*macro-* + Gr. *mastos* breast + *-ia*] oversize of the breasts or mammae.

macromazia (mak"ro-ma'ze-ah) [*macro-* + Gr. *mazos* breast + *-ia*] macromastia.

macromelia (mak"ro-me'le-ah) enlargement of one or more limbs.

macromelus (mak-rom'e-lus) [*macro-* + Gr. *melos* limb] a fetus with abnormally large or long limbs.

macromere (mak'ro-mēr) [*macro-* + Gr. *meros* part] one of the large blastomeres formed by unequal cleavage of a fertilized ovum, located in the vegetal hemisphere and dividing less rapidly than the micromeres of the animal hemisphere.

macromethod (mak'ro-meth"od) a chemical method in which the substance to be analyzed is used in customary (not minute) quantity. *Cf. micromethod.*

macromolecular (mak"ro-mo-lek'u-lar) having large molecules; pertaining to macromolecules.

macromolecule (mak"ro-mol'ĕ-kūl) a very large molecule having a polymeric chain structure, as in proteins, polysaccharides, and other natural and synthetic polymers.

Macromonas (mak"ro-mo'nas) [*macro-* + Gr. *monas* unit, from *monos* single] a genus of gram-negative chemolithotrophic bacteria of uncertain affiliation, occurring as cylindrical cells that oxidize sulfur compounds and contain sulfur granules. They are found in fresh waters with a low oxygen concentration. The type species is *M. mobilis*.

macromonocyte (mak"ro-mon'o-sīt) a very large monocyte.

macromyeloblast (mak"ro-mi'ĕ-lo-blast) a large myeloblast.

macronodular (mak"ro-nod'u-lar) characterized by large nodules.

macronormoblast (mak"ro-nor'mo-blast) a very large nucleated red blood corpuscle; macroblast.

macronucleus (mak"ro-nu'kle-us) [*macro-* + *nucleus*] 1. the larger of two types of nuclei when more than one is present in a cell. 2. in ciliate protozoa, the transcriptively active, polyploid nucleus, much larger than the micronucleus, that governs the organism's vegetative processes and is responsible for its phenotype. Called also *meganucleus*, *trophic nucleus*, and *trophonucleus*.

macronychia (mak"ro-nik'e-ah) [*macro-* + Gr. *onyx* nail + *-ia*] megalonychia.

macro-orchidism (mak-ro-or'ki-dizm) [*macro-* + Gr. *orchis* testicle] abnormal enlargement of the testis.

macropathology (mak"ro-pah-thol'o-je) [*macro-* + *pathology*] the nonmicroscopical pathologic account of any disease or organ.

macrophage (mak'ro-fāj) [*macro-* + Gr. *phagein* to eat] any of the many forms of mononuclear phagocytes found in tissues. Mononuclear phagocytes arise from hematopoietic stem cells in the bone marrow. After passing through the monoblast and promonocyte stages to the monocyte stage, they enter the blood, circulating for about 40 hours. They then enter tissues and increase in size, phagocytic activity, and lysosomal enzyme content and become macrophages. The morphology of macrophages varies among different tissues and between normal and pathologic states, and not all macrophages can be identified by morphology alone. However, most macrophages are large cells with a round or indented nucleus, a well-developed Golgi apparatus, abundant endocytotic vacuoles, lysosomes, and phagolysosomes, and a plasma membrane covered with ruffles or microvilli. Among the functions of macrophages are nonspecific phagocytosis and pinocytosis, specific phagocytosis of opsonized microorganisms mediated by Fc receptors and complement receptors, killing of ingested microorganisms, digestion and presentation of antigens to T and B lymphocytes, and secretion of a large number of diverse products, including many enzymes (lysozyme, collagenases, elastase, acid hydrolases), several complement components and coagulation factors, some prostaglandins and leukotrienes, and several regulatory molecules (interferon, interleukin-1). Among the cells now recognized as macrophages are histiocytes, Kupffer cells, osteoclasts, microglial cells, synovial type A cells, interdigitating cells, and Langerhans cells (in normal tissues) and epithelioid cells and Langerhans-type and foreign-body-type multinucleated giant cells (in inflamed tissues). **alveolar m.**, one of the rounded, granular, mononuclear phagocytes within the alveoli of the lungs that ingest inhaled particulate matter; called also *alveolar phagocyte* and *dust cell*. **armed m.'s**, those capable of inducing cytotoxicity as a consequence of antigen-binding by cytophilic antibodies on their surfaces or by factors derived from T lymphocytes. **fixed m.**, a quiescent, sessile macrophage similar to a fibroblast in morphology, found in the lymph nodes, spleen, bone marrow, and connective tissue (where it is called a histiocyte). **free m.**, an actively motile macrophage, usually having an ameboid shape and highly ruffled surface, found at sites of inflammation. **inflammatory m.**, free m.

macrophagocyte (mak"ro-fag'o-sīt) a phagocyte of relatively large size.

macrophagus (mak-krof'ah-gus) macrophage.

macrophallus (mak"ro-fal'us) [*macro-* + Gr. *phallos* penis] abnormal largeness of the penis.

macrophthalmia (mak"rof-thal'me-ah) [*macro-* + Gr. *ophthalmos* eye + *-ia*] abnormal enlargement of the eyeball.

macrophthalmous (mak"rof-thal'mus) having abnormally large eyes.

macroplasia (mak"ro-pla'ze-ah) [*macro-* + Gr. *plasis* forming + *-ia*] excessive growth of a part or tissue.

macroplastia (mak"ro-plas'te-ah) macroplasia.

macropodia (mak"ro-po'de-ah) [*macro-* + Gr. *pous* foot + *-ia*] excessive size of the feet.

macropolycyte (mak"ro-pol'e-sīt) a hypersegmented polymorphonuclear leukocyte of greater than normal size. *Cf. polycyte.*

macroprolactinoma (mak"ro-pro-lak"ti-no'mah) a prolactin-secreting pituitary adenoma of more than 10 mm in diameter and usually associated with serum prolactin levels exceeding 500 ng per milliliter.

macropromyelocyte (mak"ro-pro-mi'ĕ-lo-sīt) a very large promyelocyte.

macroprosopia (mak"ro-pro-so'pe-ah) [*macro-* + Gr. *prosopon* face + *-ia*] excessive size of the face.

macropsia (mah-krop'se-ah) [*macro-* + *-opsia*] an illusion in which objects are seen as larger than they actually are.

macrorhinia (mak"ro-rin'e-ah) [*macro-* + Gr. *rhis* nose + *-ia*] excessive size of the nose.

macroscelia (mak"ro-se'le-ah) [*macro-* + Gr. *skelos* leg + *-ia*] excessive size of the legs.

macroscopic (mak"ro-skop'ik) [*macro-* + Gr. *skopein* to examine] visible with the unaided eye or without the microscope.

macroscopical (mak"ro-skop'e-kal) 1. pertaining to macroscopy. 2. macroscopic.

macroscopy (mah-kros'ko-pe) examination with the naked eye.

macrosigmoid (mak"ro-sig'moid) [*macro-* + *sigmoid*] abnormal enlargement of the sigmoid.

macrosis (mah-kro'sis) [*macro-* + *-osis*] increase in size.

macrosmatic (mak"ros-mat'ik) [*macro-* + Gr. *osmasthai* to smell] having the sense of smell strongly or acutely developed.

macrosomatia (mak"ro-so-ma'she-ah) [*macro-* + Gr. *sōma* body] great bodily size. **m. adipo'sa congen'ita**, an obese type of premature development probably dependent on hyperfunction of the adrenal cortex.

macrosomia (mak"ro-so'me-ah) macrosomatia.

macrospore (mak'ro-spōr) [*macro-* + Gr. *sporos* seed] 1. the larger spore form when spores of two sizes are present, as in certain fungi and protozoa. 2. megaspore.

macrostereognosia (mak"ro-ste"re-o-no'se-ah) [*macro-* +

Dorland's Illustrated Medical Dictionary 27th Ed Saunders 19

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